REMARKS

I. STATUS OF THE CLAIMS

Claims 1-91 are pending, with claims 1-18, 41-43 and 63-65 currently under consideration, claims 19-40, 44-62 and 66-91 having been withdrawn as drawn to non-elected subject matter. With the Office Action mailed 30 September 2010, the Examiner has also withdrawn claims 5 and 6. With this Amendment, claims 1, 3, 6-8, 10-14 and 16 are amended, and claims 2, 41-43 and 63-65 are canceled, without prejudice against their reintroduction into this or one or more timely filed continuation, divisional or continuation-in-part applications. Thus, after entry of this Amendment, claims 1, 3-40, 44-62 and 66-91 remain pending, with claims 1, 3, 4 and 7-18 currently under consideration. The amendments of the claims and the various rejections raised in the Office Action are discussed in more detail, below.

II. AMENDMENTS

Claim 1 is amended to specify that the recombinant varicella-zoster virus comprises a BAC vector sequence and is live and attenuated. Support for these amendments can be found at least in claim 2, as well as the second full paragraph on page 2 and the first full paragraph on page 5 of the specification as filed.

Claim 2 is canceled and claims 3, 6-8, 10-14 and 16 are amended for proper dependency from claim 1.

Claim 3 is also amended to remove the phrase “at least part of” and to specify that the BAC vector sequence is inserted into a non-essential region or a region flanking the non-essential region of a varicella-zoster virus genome.

Claim 7 is also amended to recite that the BAC vector sequence comprises a recombinant protein dependent recombinant sequence selected from the group consisting of a loxP site, an FRT site, an attB site, an attP site and a res site.

Claims 11-13 are also amended to replace the phrase "is derived from" with "comprises sequences from."

Claim 14 is also amended to correct a grammatical error.

No new matter is added by way of the amendments presented herein.

VI. CLAIM REJECTIONS UNDER 35 U.S.C. §112

Claims 3, 4, 7 and 11-13 are rejected under 35 U.S.C. §112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleges that claim 3 and claims depending therefrom are indefinite, as "it is unclear how a part of the sequence can be inserted while the other part is not." (Office Action at page 4). The rejection is obviated by the amendment of claim 3.

With respect to claim 7, the Examiner alleges that it is unclear, aside from specific examples Applicants have provided on pages 46-47 of the specification, what recombinant protein dependent recombinant sequences are. Claim 7 has been amended to specify a sequence selected from a loxP site, an FRT site, an attB site, an attP site and a res site is believed to obviate this rejection, and the skilled artisan would clearly understand the scope of the claim as so amended.

The Examiner alleges that the recitation of the phrase "derived from" does not set forth the structural contents of the derived genome. Claims 11-13 have been amended to remove said phrase and to specify that the varicella-zoster virus genome comprises sequences from a wild type strain, a mutant type strain, and an Oka vaccine strain, respectively.

In light of the above, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

V. CLAIM REJECTIONS UNDER 35 USC §102

Claims 1-4, 8-12, 17, 18, 41-43 and 63-65 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Horsburgh *et al.* (US Patent 6,277,621 B1, hereinafter "Horsburgh"). This rejection is respectfully traversed.

A. The Present Claims

Claim 1, as amended, relates to a live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence.

B. The Cited Art

HORSBURGH describes a bacterial artificial chromosome (BAC) construct, comprising a viral nucleic acid that directs the formation of a recombinant virus in the cell, wherein one example of the virus can be Varicella-Zoster virus (VZV).

C. Analysis

The standard for lack of novelty, that is, for anticipation, is one of strict identity. According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as it is contained in the claim." *See Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Moreover, the knowledge must be sufficiently enabling to place the information in the possession of the public. *See In re Omeprazole Patent Litigation*, 82 USPQ2d 1643 (Fed. Cir. 2007).

Horsburgh features an artificial chromosome construct containing a nucleic acid sequence that directs formation of a recombinant virus (e.g., a lytic or a non-lytic virus) upon introduction into a cell. Horsburgh teaches introduction of foreign nucleic acid sequences into a bacterial artificial chromosome construct, with a primary focus on the introduction of Herpes Simplex Virus (HSV) into a BAC, as means of production of recombinant HSV in cells, in gene therapy methods, or in vitro, for example, in recombinant virus production methods or in amplicon packaging. Again, Horsburgh teaches introduction of a viral sequence into a BAC, rather than the reverse. The only teaching in Horsburgh remotely related to an attenuated virus is in column 5, lines 4-10, in which the possibility of expressing a mutated virus is considered. However, this passing mention using artificial chromosome constructs to produce an attenuated or mutated virus from the BAC so that the virus does not replicate and/or so that it cannot kill the cell in which it is produced by, for example, inducing lysis or apoptosis of the cell fails to rise to the level of conception of, or enabling teaching of Applicants' fully conceived, specifically described, enabled and claimed live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence.

Accordingly, Applicants submit that standard of strict identity to maintain a rejection under 35 U.S.C. § 102 has not been met and withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested.

VI. CLAIM REJECTIONS UNDER 35 USC §103

Claims 13, 14 and 15 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Horsburgh in view of the English translation of the abstract of PCT Publication WO 00/50603 to Gomi *et al.* (hereinafter, "Gomi abstract").

Claims 7 and 16 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Horsburgh in view of Mori *et al.* (US Patent Application Publication 2008/0226677, filed May 12, 2004, hereinafter "Mori").

A. The Rejected Claims

Claims 13, 14 and 15 relate to a live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence, wherein:

the varicella-zoster virus genome comprises sequences from an Oka vaccine strain (**Claim 13**);

the varicella-zoster virus genome has mutations in gene 62 and gene 6 (**Claim 14**);

the gene 62 comprises at least certain base substitutions in SEQ ID NO. 5 (**Claim 15**).

Claims 7 and 16 relate to a live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence, wherein the BAC vector sequence comprises:

a recombinant protein dependent recombinant sequence selected from the group consisting of a loxP site, an FRT site, an attB site, and attP site and a res site (**Claim 7**);

the sequence set forth in SEQ ID NO.: 7 (**Claim 16**).

B. The Cited Art

Horsburgh is discussed above.

GOMI ABSTRACT describes an attenuated chicken-pox virus Oka strain gene 62 having a specific sequence and particular base substitutions as a vaccine; and a method for identifying the attenuated chicken-pox virus Oka strain and an attenuated chicken-pox virus strain acceptable as a virus strain for attenuated live chicken-pox vaccine.

MORI describes a recombinant herpes viral vector for introducing a desired gene into lymphoid cells, and a method for producing a recombinant herpesvirus using a vector comprising a herpesvirus genomic gene and a BAC vector sequence, a cell comprising the vector, and a nucleic acid cassette comprising a fragment, which is capable of homologous recombination with a herpesvirus genome.

C. Analysis

C1. Legal Standard for Determining Obviousness Under 35 U.S.C. § 103(a)

Determining obviousness under 35 U.S.C. § 103(a) requires an objective analysis involving four factual inquiries, which include:

(a) determining the scope and content of the prior art,

(b) ascertaining the differences between the prior art and the claims at issue;

(c) resolving the level of ordinary skill in the art; and

(d) evaluating evidence of secondary considerations.

See Graham v. John Deere, 383 US 17, 18, 148 USPQ 459, 467 (1966); *see also* M.P.E.P. § 2141. A claim composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1385 (US 2007). It is also important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *See id.* Thus, in assessing the scope and content of the prior art, the references must be considered in their entirety, *i.e.*, each as a whole including portions that would lead away from the claimed invention. *See W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 US 851 (1984); *see also* M.P.E.P. § 2141.02.

Further, the Office examination guidelines following the Court decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1385 (US 2007) indicate that an issue to consider in assessing obviousness is whether a combination of prior art elements yields "predictable results." *See Federal Register*, Vol. 72, No. 195, October 10, 2007.

The problem Applicants' set out to solve was to develop a safe, effective attenuated live varicella vaccine with increased homogeneity, superior to VZV vaccines based on the Oka strain, known in the art. Applicants achieved this objective with provision of a live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence.

With respect to claims 13-15, the Examiner acknowledges that, while Horsburgh does not disclose the mutations in genes 62 and 6 as claimed, the combination of Horsburgh with the Gomi abstract provides the missing teaching, because "(i)t would have been obvious to have used all of the attenuating mutations of the attenuated Oka strain of the WIPO abstract" and that "One would have been motivated to use all of the mutations in order to ensure its safety as a vaccine." (Office Action at page 7).

However, as noted above, Horsburgh was not even focused on insertion of a BAC vector sequence into a non-essential gene of varicella-zoster virus to achieve Applicants' live, attenuated virus comprising a BAC vector sequence. Gomi characterizes a particular attenuated chicken-pox virus Oka strain gene 62 and conceives of its use as a vaccine. Nothing in the Gomi abstract teaches or suggests disruption of non-essential genes using a BAC vector, much less provides any coherent teaching of Applicants' live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence, and the skilled artisan would not have been directed in any way to combine Horsburgh with the Gomi abstract, because neither reference conceived of making a live, attenuated virus comprising a BAC vector sequence.

With respect to claims 7 and 16, the Examiner alleges that Mori discloses a recombinant protein dependent recombinant sequence, and although Horsburgh does not disclose such a sequence, "it would have been obvious to have used any other available BAC vector sequence, such as the sequence taught by Mori as SEQ ID NO: 401 (100% identical to Applicant's SEQ ID NO: 7)." (Office Action at pages 7-8).

In fact, Mori discusses viral gene transfer using a recombinant herpes viral vector for introducing a desired gene into lymphoid cells, rather than Applicants' presently claimed live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence, wherein the BAC vector sequence comprises a recombinant protein dependent recombinant sequence selected from the group consisting of a loxP site, an FRT site, an attB site, and attP site and a res site. Mori is not directed to the use of a BAC vector to produce an attenuated virus. Again, the skilled artisan would not have made the combination of Mori with Horsburgh, and even assuming, *arguendo*, that the skilled artisan did happen to make the combination, she would not have arrived at Applicants' presently claimed live attenuated virus, as neither reference teaches this concept with any particularity.

Applicants submit that, in contrast to the Examiner's assertions, when considered as a whole, in no way does Horsburgh lead one to modify the disparate teachings of a BAC vector containing a foreign nucleic acid sequence therein to achieve Applicants' live attenuated virus comprising a BAC vector sequence. Moreover, the secondary references, Gomi and Mori, fail to make up for the deficiencies of Horsburgh. Specifically, neither reference provides even a remote suggestion of using a BAC vector to disrupt the particularly claimed non-essential gene to arrive at a live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence having particular recombinant protein dependent recombinant sequences of claims 7 and 13-16. None of the references, when considered either singly or in combination, teaches or

suggests the live, attenuated recombinant varicella-zoster virus comprising a BAC vector sequence wherein the BAC vector sequence comprises either (1) a recombinant protein dependent recombinant sequence selected from the group consisting of a loxP site, an FRT site, an attB site, and attP site and a res site, or (2) specific mutations in gene 62 and gene 6 as encompassed by Applicants' claims 7 and 13-16.

For the reasons discussed above, the Applicants submit that the claimed subject matter patentably defines over the cited references, and respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

VII. DOUBLE PATENTING

Claims 1-4, 7-18, 41-43 and 63-65 were provisionally rejected under the judicially created doctrine of nonstatutory obviousness-type double patenting as allegedly being directed to an invention not patentably distinct from claims 1, 4, 11 17, 24 and 25 of co-pending Application No. 12/094,757.

As noted by the Examiner on page 9 of the Office Action, this rejection is provisional precisely because the claims of the 12/094,757 application have not, in fact, been patented. It would be improper for the Examiner to maintain a provisional obviousness-type double-patenting rejection based on claims that have not been allowed or issued in a patent.

Until patentable subject matter is found in the applications not yet granted and serving as the basis of the provisional rejections under the judicially created doctrine of obviousness-type double patenting, the claims of the instant application should be considered on their merits. Furthermore, as stated in the Manual for Patent Examining Procedure, "(i)f the 'provisional' double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw the rejection and permit the application to issue as a patent" (M.P.E.P. 804(I)(B)).

Applicants respectfully request that the claims of the instant application be considered on their merits, and further request that the provisional rejection be held in abeyance until the other rejections in this case are overcome and the claims of this case are otherwise in condition for allowance. Applicants reserve the right to file a terminal disclaimer in the event that it is deemed necessary in a later stage of prosecution.

VIII. CONCLUSION

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for Allowance. A Notice of Allowance is therefore respectfully requested.

No fees, beyond the fee for a one-month extension of time, are believed to be due in connection with this Amendment. However, the Commissioner is authorized to charge any additional fees that may be required, or credit any overpayment, to King & Spalding LLP Deposit Account No. 50-4616.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 590-1932.

Respectfully submitted,

Date: 31 January 2011

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